



## ATTACHMENT A Remarks

Claims 1-17 stand pending in the present application. By this Amendment, Applicants have amended claim 13 and added new claim 17. Applicants respectfully submit that the present application is in condition for allowance based on the discussion which follows.

The Examiner acknowledged Applicants' election with traverse of Group I. During Applicants' traverse, Applicants argued that dependent claims 3-9 and 12 which depend from claim 1 should be considered part of Group I as being species of the generic independent claim 1. However, the Examiner maintains the Restriction Requirement.

Applicants reiterate their position and dispute the Examiner's contention that dependent claims 3-9 and 12 are directed to a different target compound which is different in structure and functionality. Dependent claims 3-9 and 12 although including a further initial step, are not a separate invention in accordance with U.S. Restriction Requirement practice. Since claims 3-9 and 12 are dependent from claim 1, claims 3-9 and 12 are species of the generic independent claim 1. Accordingly, should claim 1 be found to be allowable, dependent claims 3-9 and 12 necessarily would be allowable. Therefore, it is inappropriate to restrict claims 3-9 and 12 from the present application. Should the Examiner continue to maintain the restriction, Applicants reserve the right to file a divisional application on the Examiner's deemed withdrawn claim 3-9 and 12.

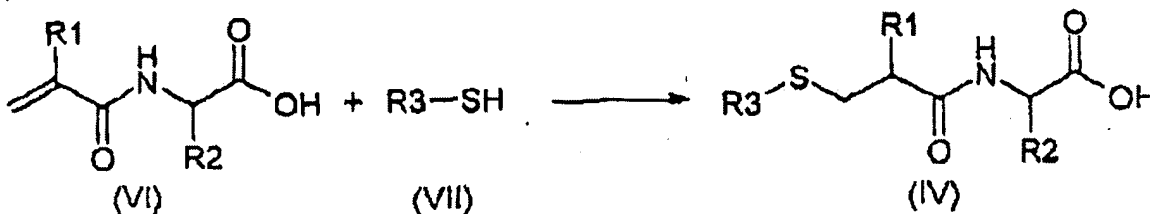
Claim 13 was rejected under 35 U.S.C. § 112, second paragraph, for including the phrase "chirality inducers" alleging that it is not clear which of the multiple chiral

compounds in the art can satisfy the claim limitations. By this Amendment, Applicants have amended claim 13 by replacing the phrase "chirality inducers" with "quinquina alkaloid or derivatives thereof". Subject matter support for this expression is found in the specification as filed, e.g., page 14, line 37 to page 15, line 4. Accordingly, the amendment to claim 13 is not indefinite and does not constitute new matter. Applicants respectfully request that the rejection to claim 13 under 35 U.S.C. § 112, second paragraph, be withdrawn.

Claims 1, 2, 10, 11 and 14-16 were rejected under 35 U.S.C. § 103(a) as being obvious over Greenberg et al U.S. Patent Nos. 4,401,667 or 4,474,799 (hereinafter collectively referred to as "Greenberg et al"). The Examiner alleges that Greenberg et al discloses a preparation which produces derivatives of formula (I). However, the Examiner admits that Greenberg et al does not use the claimed ester of acrylamide (VI) nor does Greenberg et al prepare compounds outlined in claims 15 and 16.

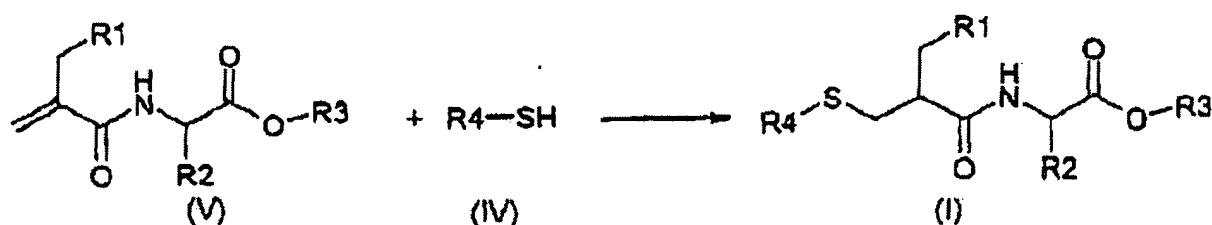
First, Applicants respectfully note that the Examiner has failed to make a prima facie case of obviousness. The Examiner merely makes a declaratory statement that the aforementioned claims are obvious in view of Greenberg et al. For example, the Examiner has failed to explain why he believes the claimed ester coupling reaction would be obvious from Greenberg et al which teaches an acid coupling.

Greenberg et al discloses the following

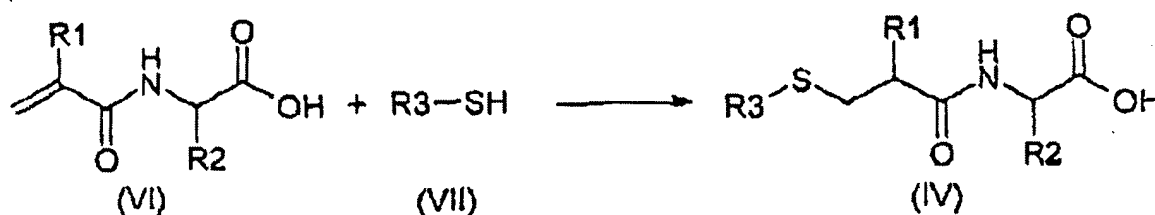


It is apparent that Greenberg et al specifically discloses the coupling reaction with acid derivatives (VI).

Second, even assuming a prima facie case of obviousness has been raised in the Office Action, the present invention is not obvious from Greenberg et al. In sharp contrast to Greenberg et al's acid coupling reaction, the present claims refer to the following reaction:



in which R3 represents a lower alkyl group or a lower phenylalkylene group. It is clearly apparent that the present claims do specifically refer to a reaction with ester derivatives (V) and not a reaction with acid derivatives of Greenberg et al.



Moreover, it would not have been obvious to one of ordinary skill in the art to substitute the present reaction with ester derivatives for the reaction with acid derivatives of Greenberg et al. It was previously submitted in the Declaration by Mr. Danvy that at the time of the present invention, there existed a prejudice against the ester reaction of the present claims, in particular, in terms of yields and purity of the obtained product. Namely, one of ordinary skill in the art would have expected higher

yields and higher purity from a reaction with acid derivatives than from a reaction with ester derivatives. (See Declaration Under Rule 132 submitted with the December 4, 2000 Amendment.) Greenberg et al fails to provide any motivation or suggestion in the art to substitute an ester reaction for its acid reaction which would have been counter to the conventional teaching at the time.

By this Amendment, to further support the non-obviousness of the present invention, Applicants submit a Second Declaration Under Rule 132. In the Second Declaration, Mr. Danvy demonstrates that the present unlikely reaction based on conventional teaching produces enhanced products in terms of yield and purity as compared with the prior art of Greenberg et al. See, e.g., Second Declaration, Sections 3 and 5. To demonstrate that the present method provided higher yields and enhanced purity, Applicants compared the product prepared using the Greenberg et al method with that of the present method. See Second Declaration, Sections 2 and 3.

Contrary to conventional thinking, the present inventors have unexpectedly provided a reaction allowing a coupling with higher yields and easier implementation into industrial applications. See Second Declaration, Sections 3 and 4. Consequently, the reaction of the present claims exhibits great and unexpected advantages over the prior art.

Further, one of ordinary skill in the art would not have reasonably expected the aforementioned advantages in view of the common general knowledge at the time and the prior art. See Second Declaration, Section 6.

Furthermore, Greenberg et al does not provide an enabling disclosure for one of ordinary skill in the art to practice the present ester coupling. The teaching of

Greenberg et al is clearly limited to the acid derivatives. In the relevant passage in column 3, lines 25-50, Greenberg '677 discloses a preparation of starting product of formula (VI) from intermediate of formula (IV) and (V). In order for a reference to be anticipatory or to make an invention obvious, the reference must be enabled which requires that the "prior art reference must teach one of ordinary skill in the art to make or carry out the claimed invention without undue experimentation" (Elan Pharm. Inc. v. Mayo Found., 68 U.S.P.Q.2d 1373 (Fed. Cir. 2003)). Clearly, Greenberg et al fails to suggest an ester coupling let alone enable one of ordinary skill in the art to conduct such a coupling where Greenberg et al is clearly linked to acid derivatives.

It is further noted that Greenberg et al actually teaches from carrying out the coupling reaction with an ester derivative. In sharp contrast to Greenberg et al, the present obtained product is in the form of an ester group. Nevertheless, Greenberg et al specifically teaches the skilled person to remove the ester group to obtain the acid derivative of formula (VI).

Based on the foregoing, Applicants respectfully submit that claims 1, 2, 10, 11 and 14-16 are not obvious in view of Greenberg et al. Accordingly, Applicants respectfully request that the Examiner withdraw the rejection to claims 1, 2, 10, 11 and 14-16.

Applicants gratefully appreciate the Examiner's indication of allowable subject matter of claim 13 which would be allowed if rewritten to overcome the 35 U.S.C. § 112, second paragraph, rejection and in independent form. By this Amendment, Applicants have added new claim 17 which corresponds to claim 13 rewritten in independent form and includes the corresponding change reflected in claim 13 (currently amended) as

discussed above. Accordingly, Applicants respectfully submit that claim 17 is allowable as being in accordance with the indication of allowable subject matter of the Office Action.

In view of the foregoing, Applicants respectfully submit that the application is in condition for allowance.

**END REMARKS**